

REMARKS

Applicants gratefully acknowledge the Examiner's indication that a method is enabled for inducing a T-cell or B-cell mediated immune response to PAP in a mammal, wherein the method comprising intramuscular, intravascular, intravenous, or intra-arterial administration of the recombinant pTVG or vaccinia virus construct comprising a polynucleotide PAP sequence linked to a promoter. Applicants also gratefully acknowledge the indication in the Office Action that Claims 25 and 29 are free of the prior art.

The Office Action, however, rejected claims 1-9, 23-25, 28-30 and 32, asserting that they lack enablement under 35 U.S.C. §112, ¶1. Applicants respectfully traverse the rejection.

As an initial matter, "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988), *see also In re Wands*, 858 F.2d 731, 737, (Fed. Cir. 1988), and MPEP § 2164.01.

The Office Action first asserted that the claims are not enabled because they recite a method for inducing immune reaction, yet the specification only exemplifies humoral and cellular immune reactions, without indicating for example whether innate immune responses are also induced. Applicants respectfully submit that the Office Action used an improper legal standard in reaching the conclusion of non-enablement. As an initial matter, the disclosure in the specification teaches, to one ordinarily skilled in the art, that the claimed method does induce an immune reaction, and whether the method induces all immune reactions is not relevant to the enablement analysis. With regard to innate immune reactions, whether they are induced by the claimed method can be determined easily by one of ordinary skills in the art. If it does, then it is encompassed by the claim. More importantly, even if the claimed method does not induce innate immune reaction, the claims are still enabled. This is because

[t]he presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling).

MPEP §2164.08(c). In the instant case, one of ordinary skills in the art would readily recognize that the for all practical purposes (that is, for killing cancer cells or other therapeutic purposes), humoral and/or cellular immune response is all that matters. It is irrelevant whether innate immune reactions are also involved. An analogy can be made to a claim reciting "A method of operating a car," where the specification only discloses how to operate the car on a road or other solid surfaces. There is no need to specify in the claim that the car must be operated on a solid surface, because one of ordinary skills would be able to determine, without undue experimentation, that the inoperative subject matter (e.g. operating the car on the surface of water) is excluded. Therefore, the lack of information regarding whether innate immune reactions are induced by the claimed method does not make the claims non-enabled and there is no need to limit the claims to the specifically exemplified immune reactions.

In order to expedite prosecution and advance this application to allowance, applicants have nevertheless amended the claims to recite that the method is used to induce a humoral or cellular immune reaction, thereby rendering the above rejection moot. It is explicitly stated that this amendment is made without acquiescing to the assertions in the Office Action.

Secondly, the Office Action asserts that because of the unpredictability of "successful" treatment method (citing Hu et al., 1998), and the lack of any working examples, the claims related to method of prostate cancer treatment are not enabled. Applicants note that for the claimed method to be enabled, the

method does not necessarily have to be able to cure cancer, so evidence of cancer regression is not necessary for enablement. One of ordinary skills in the art would recognize that the claimed method is useful in cancer treatment, and he or she can “make and use” the claimed invention without any undue experimentation. There is no reason to believe that the method will not help cancer treatment, and *in vivo* or clinical data is not necessary for patentability analysis. In any event, applicants have generated additional data, attached as **Exhibit I**, showing that the method inhibits tumor growth *in vivo*. The data will be provided in the form of a declaration under 37 C.F.R. § 1.132 by the applicants if the Examiner deems it necessary.

The Office Action next asserts that the specification has not enabled all possible routes of administration, but only exemplifies the use of a particular plasmid and a vaccinia virus, and it would take undue experimentation to test other types DNA constructs and transcriptional regulatory elements. Applicants respectfully submit that this assertion is again improper. Even if it is scientifically sound to doubt the viability of other, non-exemplified administrative routes, the claimed invention remains enabled, because, as discussed above, that the claims may encompass “inoperative subject matter.” More importantly does not make them nonenabled. Regardless, the assertion that only plasmid or vaccinia viral vectors are suitable for the claimed method is not scientifically sound.

The Office Action cited and relied on certain languages in a few references, all of which was published in 1997 or earlier, for the notion that a factor that affect efficient gene delivery and sustained gene expression is the need for appropriate vector/promoter combination for a particular cell type, and the search for such a combination is a case of “trial and error.” These references, however, do not state that undue experimentation would be required. Even if a “trial and error” approach was used, it is not evidence that such an approach necessarily requires undue experimentation. In fact, these references merely show that it is routine in the art to engage in these kind of efforts.

Furthermore, substantial progress has been made in this hot area of scientific research. In the area of gene therapy, a great number of successes, both *in vitro* and *in vivo*, have been documented with other types of expression vectors, notable of which is the adenoviral vectors. For example, even the Verma et al. (1997, Nature 389: 239–242) reference, heavily relied upon by the Office Action, states that “adenoviral vectors are extremely useful if expression of the transgene is required for short periods of time. One promising approach is to deliver large numbers of adenoviral vectors containing genes for enzymes that can activate cell killing... to cancer cells. In this case, the cellular immune response will augment tumor killing.” Verma et al. at 241, col. 2.

As further evidence that the Office Action used improper legal standards in the asserted lack of enablement rejection, the U.S. PTO has allowed many claims where the specification exemplifies only one or two types of vectors, while the issued claims have no limitation on the vector/promoter combination. See e.g. U.S. Pat. No. 6,214,804 (particularly Claim 3).

Applicants further submit that the rejection as non-enabled with regard to the method of administration is also improper. It is incorrect for the Office Action to state that the specification “fails to provide guidance on any method of administration of vector encoded PAP in order to induce an immune response,” because the specification provides specific examples with regard to many administration methods. It is true oral or topical routes are not specifically exemplified, but there is no evidence that to a person of ordinary skills in the relevant art, “making and using” the claimed invention would require undue experimentation. To the extent that a theoretically possible administration method encompassed in the claims is inoperative, the claims are not rendered non-enabled as a consequence, as determining whether certain method is or is not operative requires no undue experimentation.

In short, it is respectfully submitted that the claim rejections under 35 U.S.C. § 112, ¶ 1 for lack of enablement are improper and should be withdrawn.

Double Patenting

It is respectfully submitted that the claim objection due to Claims 30 and 32 being substantially duplicative has been rendered moot by the amendment of Claim 32, making it dependent from Claim 26, instead of from Claim 23.

Claim Rejection under 35 U.S.C. § 102(e)

The Office Action also rejected all claims under consideration other than Claims 25 and 29 for lack of novelty, citing Houghton et al. (U.S. Pat. No. 6,328,969). Applicants respectfully traverse.

It is respectfully submitted that Houghton et al. does not in any way disclose a method of delivering a DNA construct encoding PAP into a patient for the treatment of cancer or induce an immune reaction. It merely discloses broadly and generically the use of differentiation antigen for induction of immune responses. The pin-point citation to the specification of Houghton et al. is difficult to locate as the issued patent does not use paragraph numbers. To the best ability of the undersigned in locating the paragraphs as referred to in the Office Action, neither Claim 1, nor ¶ 6 or any adjacent paragraphs, nor anywhere in the entire Houghton et al. document, discloses a DNA construct expressing PAP, as an antigen. There is no disclosure in the Houghton et al. reference that a recombinant DNA construct comprising a polynucleotide sequence encoding PAP operatively linked to a transcriptional regulatory element, and that when administered to a mammal, the mammal develops an immune reaction to PAP. Because a "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference," *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987), Houghton et al. does not anticipate the instantly claimed invention. This rejection is especially improper in view of the reasoning used in the Office Action in asserting the lack of enablement of the claims.

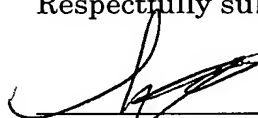
In summary, applicant respectfully submits that all claims are in condition for allowance and earnestly solicit an early indication from the

Examiner to that effect. If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

This reply is timely by virtue of the concurrently filed herewith Petition for Extension of time and the requisite fees. However, if additional time should be needed, this reply should be construed as an additional petition and the Commissioner is authorized to charge any additional fee to Deposit Account No.

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Respectfully submitted,



Kening Li, Ph.D.
Registration No. 44,872

CROWELL & MORING LLP
Intellectual Property Group
P.O. Box 14300
Washington, DC 20044-4300
Telephone No.: (202) 624-2500
Facsimile No.: (202) 628-8844
KL

#380196